PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
A000005		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP00/09858	05/10/2000	07/10/1999
International Patent Classification (IPC) or national classification and IPC A61K31/195		
Applicant WARNER-LAMBERT COMPANY et al.		

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A0000005/1-01-MG

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
27/04/2001	11.07.2001
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Pilling, S Telephone No. +49 89 2399 8461

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP00/09858

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
Description, pages:

1-20 as originally filed

Claims, No.:

1-18 as originally filed

Drawings, sheets:

1/16-16/16 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 1-9.

because:

☒ the said international application, or the said claims Nos. 1-9 relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reason d statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N) Yes: Claims 1-18

	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-18
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	10-18 (for claims 1-9 see the comments under Item V on separate sheet)
	No:	Claims	

2. Citations and explanations
see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. Claims 1 to 9 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

2. The present application relates to treatment of chronic pain using a synergistic combination of an NK_1 receptor antagonist and a GABA analogue (Claims 1 to 9 and 18); pharmaceutical compositions comprising a synergistic combination of an NK_1 receptor antagonist and a GABA analogue (Claims 10 to 17).

3. Claims 1 to 9 relate to methods of treatment of the human or animal body by therapy. In this regard, for the assessment of these claims with respect to industrial applicability, no unified criteria exist in the PCT. Furthermore, patentability can be dependent on the formulation of the claims. The EPO, for example does not recognize as industrially applicable, the subject matter of claims directed to a method of treatment of the human or animal body or to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

4. The documents cited in the International Search Report (ISR) are consecutively numbered D1 to D4 in the order of their listing. If not indicated otherwise, reference is made to the passages cited in said ISR.

5. None of the documents discloses combinations of an NK_1 receptor antagonist and a GABA analogue. Thus, the subject matter of the present claims is new (Article 33(2) PCT).

6. The closest prior art in respect of the present claims appears to be any of documents D1 to D3. These documents show that the separate use of either (i) NK_1 receptor analogues such as CI-1021 (see documents D1 and D2) or (ii) GABA analogues such as gabapentin or pregabalin (see document D3) for the treatment of conditions involving chronic pain is known. According to the evidence in present Examples 1 and 2, the Applicant has shown that NK_1 receptor analogues in combination with GABA analogues have a synergistic effect in controlling chronic pain. This results in an enhanced therapeutic effect and/or dosage reduction. Hence, the objective technical problem to be solved by the subject matter of the present application appears to be "how to provide compositions for controlling chronic pain with enhanced therapeutic effect or compositions with similar therapeutic effects but reduced dosages of active agents". There seems to be no teaching in any of the present prior art documents that the latter technical problem could be solved by combining NK_1 receptor antagonists with GABA analogues or that any synergistic effects would result from this combination. Hence, the disclosure of the present application appears to make an inventive contribution to the art. Thus, the subject matter of Claims 1 to 18 appears inventive (Article 33(3) PCT).

7. With reference to the disclosure of document D4, it is noted that (i) the publication date of document D4 (January 2000) is after the present earliest declared priority date (07.10.1999) and (ii) the subject matter of the present claims appears to be entitled to the benefit of said earliest declared priority date of 07.10.1999. Hence, the disclosure of document D4 does not comprise part of the state of the art for the purposes of assessment of novelty and inventive step under the PCT.